objection. In Preparation Example 1 of the present specification (pages 15 and 16), the Vacutainer® tubes are clearly described as "collection tubes" and "evacuated specimen tubes". Specification at page 16, line 1 and page 15, line 29.

In light of the foregoing, it is respectfully requested that the Examiner reconsider and withdraw his objections to the manner of trademark usage in this application.

II. Rejections Under 35 U.S.C. § 112, Second Paragraph.

The Examiner has rejected claims 1-22 under 35 U.S.C. § 112 as indefinite for various reasons. Each rejection is addressed below in the order discussed by the Examiner.

The Examiner has rejected claim 1 as indefinite, asserting that the claim contains "functional limitations" which are, according to the Examiner, improper for a claim directed to a composition. The applicants respectfully traverse this rejection.

A functional limitation in a composition claim is perfectly acceptable if it sets definite boundaries on the patent protection sought. M.P.E.P. 2173.05(g), citing *In re Barr*, 44 F.2d 588. Claim 1 is directed to an injectable material comprising cross-linked, blood plasma proteins for soft tissue augmentation. The claim contains elements defined in terms of both structure and function. Use of functional definitions to teach the metes and bounds of a claimed invention to artisans of ordinary skill in the art is perfectly acceptable under U.S. patent law, and is often more effective than mere recitations of structure. *Id.* Thus, it is respectfully requested that the Examiner reconsider and withdraw his § 112 rejection of claim 1.

The Examiner has specifically rejected claims 5 and 6 as indefinite for use of the language "wherein the . . . proteins are purified and sterilized" and "wherein the . . . proteins are dialyzed and autoclaved", asserting that such language is superfluous. The applicants respectfully traverse this rejection.

The Examiner's rejection is premised on his apparent assumption that the term "injectable", as used in claim 1, encompasses sterilization and purification processes. This is incorrect; the term "injectable" as used by the applicants indicates that the material is capable of being delivered to the patient by syringe or needle, for example. *See, e.g.*, Preparation Example 1. Thus the terms "sterilized", "purified", "autoclaved" and "dialyzed" are additional elements

and therefore properly included in dependent claims 5 and 6. It is therefore requested that the Examiner reconsider and withdraw his § 112 rejection as applied to claims 5 and 6.

The Examiner has rejected claims 9 and 11 as indefinite for use of the language "providing". Claims 9 and 11 have been amended to delete this language and to substitute "obtaining". Accordingly, it is respectfully requested that the Examiner reconsider and withdraw his § 112 rejections of claims 9 and 11.

Finally, the Examiner has rejected claim 22 as indefinite, asserting that it fails to disclose an endpoint for the process treatment and the amount of material to be injected. The applicants respectfully traverse this rejection.

A claim is not indefinite if, interpreted in light of the disclosure, it reasonably apprises a person of ordinary skill in the art of the invention. M.P.E.P. 2106(v)(A). It is well known in the art that the dosages and the duration of injectable tissue augmentation therapies, such as the collagen injections of the prior art, are variable and depend upon numerous patient-specific criteria such as degree of skin damage, the age of the patient, the anatomical location of the skin being treated and the aesthetic preference of the patient. Thus, the claimed invention is not indefinite, as one of ordinary skill in the art would easily recognize that the dosage and the duration of treatment could be routinely determined based upon the usual patient-specific criteria.

In light of the foregoing, it is respectfully requested that the Examiner reconsider and withdraw his § 112 rejections of claims 1–22.

III. Rejection Under 35 U.S.C. § 102(b) Based Upon Coleman or Pollack.

The Examiner has rejected claims 1, 5, 6, 8 and 22 as anticipated based upon Coleman *et al.*, eds., *Skin Resurfacing* pp. 217-234 (1998) ("Coleman"). Similarly, the Examiner has rejected these same claims as being anticipated by Pollack, *Silicone, Fibrel, and Collagen Implantation for Facial Lines and Wrinkles,* J. Dermatol. Surg. Oncol., vol. 16, no. 10, pp. 957-961 (October 1990) ("Pollack"). The applicants respectfully traverse these rejections for the reasons discussed below.

In order for a cited reference to anticipate a claimed invention, the reference must teach each and every element of the claimed invention. M.P.E.P. 2129. Coleman teaches a composition for treating wrinkles and scars which contains a mixture of porcine gelatin powder

(collagen), sterile saline, and ε-amino caproic acid, which is mixed with a patient's plasma prior to injection. The fluid plasma acts as a carrier for the porcine collagen injection. The Coleman composition is marketed under the name "Fibrel®". Similarly, Pollack teaches use of the same Fibrel® composition for the amelioration of facial lines and wrinkles.

Contrary to the Examiner's assertion, neither Coleman nor Pollack anticipates the claimed invention, as neither teaches an injectable material for tissue augmentation comprising cross-linked, blood plasma proteins. That the plasma carrier fluid disclosed in the references may incidentally contain blood plasma proteins is irrelevant, as such proteins are not cross-linked and therefore remain soluble. In contrast, the injectable material of the present invention contains cross-linked, blood plasma proteins which are insoluble and non-biodegradable, and can therefore act as filler to augment the treated tissue. Accordingly, because Pollack and Coleman do not teach each and every element of the claimed invention, they cannot anticipate it. It is respectfully requested that the Examiner reconsider and withdraw his § 102 rejection.

IV. Rejection Under 35 U.S.C. § 103(a) Based Upon Coleman or Pollack in View of Other References.

The Examiner has rejected claims 1-22 as being obvious over Coleman or Pollack in view of:

(1) Grabek *et al., Analytical Biochemistry*, vol. 185, pp. 13-135 (1990) ("Grabek"); or

(2) Wong, *Chemistry of Protein Conjugation and Cross-linking*, pp. 39-40 and 195-207 (1991) ("Wong"); or

(3) Wang *et al., Journal of Parenteral Drug Assoc.*, vol. 34, no. 6, pp. 452-462 (Nov.-Dec. 1980) ("Wang").

The Examiner asserts that Grabek teaches use of crosslinking agents for the purpose of crosslinking protein-protein complexes, including use of zero-length crosslinking procedure. Wong, according to the Examiner, teaches various zero-length cross-linking reagents for the purpose of creating stable bonds between two intrinsic chemical moieties of one or more polypeptide chains. Finally, the Examiner contends that Wang teaches numerous physiologically acceptable fluids as additives for parenteral formulations, including anesthetic compounds. None teaches, discusses, or suggests use of the disclosed processes or reagents to produce an

injectable material for tissue augmentation comprising cross-linked blood plasma proteins. Thus, the applicants traverse this rejection for the reasons outlined below.

To establish a *prima facie* case of obviousness based upon a combination of references, the Examiner must show: (1) that the combination of references teaches or suggests all elements of the invention as claimed; (2) that there is in the art a motivation or suggestion to make such combination; and (3) that a person of ordinary skill in the art would have a reasonable expectation that such combination would be successful.

In the present case, the Examiner has failed to satisfy all of the above requirements for a *prima facie* case of obviousness. First, none of the six combinations put forth by the Examiner teaches or suggests all of the elements of the claimed invention. As discussed in the prior section of this response, neither Coleman nor Pollack, the "primary" references, teaches an injectable material comprising cross-linked blood plasma proteins. The mere addition of the zero-length crosslinking of Grabek and/or Wong does not remedy this deficiency. Similarly, the combination of the physiologically acceptable fluids taught by Wang with the teachings of Coleman and/or Pollack, as suggested by the Examiner, does not disclose an injectable material comprising cross-linked blood plasma proteins, as required by the present invention.

Additionally, even if the Examiner's suggested combinations did teach or suggest each and every element of the claimed invention, which they do not, such combinations do not render the claimed invention obvious, for there was no motivation or suggestion in the art to combine the references as suggested by the Examiner to arrive at the present invention. Both Coleman and Pollack teach the use of collagen (porcine gelatin powder), a natural structural tissue, as a filler substance for the amelioration of skin imperfections, such as scars or wrinkles. In contrast, the present invention utilizes blood plasma proteins, ordinarily soluble and biodegradable within the body, as the filler substance. There would have been no motivation or necessity to combine the teachings of Coleman or Pollack with those of Grabek, Wong or Wang to arrive at the present invention comprising filler crosslinked blood plasma proteins, as Coleman and Pollack already teach use of a totally different filler, namely collagen.

Finally, there is no that a person skilled in the art would have had a reasonable expectation of success in combining these references, particularly in view of the differences

between the fillers of Coleman and Pollack, one the one hand, and the various fluids taught by the secondary references.

Accordingly, for the reasons given above, it is respectfully requested that the Examiner reconsider and withdraw his § 103 rejection.

CONCLUSION

In light of the foregoing amendments and remarks, it is respectfully submitted that the present claims and specification are fully compliant with § 112, and, in light of the foregoing remarks, it is respectfully submitted that the claims are patentably distinguished over all art of record and known to applicants. Reconsideration and allowance of the claims are earnestly solicited.

Respectfully submitted,

NORMAN ORENTREICH, *et al.*

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(Date)

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